## REMARKS

For convenience, the Examiner's rejections are addressed in the order in which they were presented in the October 28, 2002, Office Action.

**Status of the Claims**

With this amendment, claims 1-41 are pending in the present application and under examination. Claims, 1, 27, and 35 are amended. Appendix A provides the version with markings to show change to the amended claims. Appendix B shows all pending claims under examination after entry of the present amendments.

**Amendment to the Claims**

No new matter has been added by the present amendments.

Claim 1 has been amended to more clearly reflect the claimed invention. Support for this amendment can be found, for example, on page 1, lines 7-8 of the specification and in the claims as filed.

Claims 27 and 35 have been amended to provide the correct dependency. Support for these amendment can be found in the claims as filed.

Claim amendments are for purposes of improved clarity or consistency of claim language unless otherwise noted. No claim amendment should be construed as an acquiescence in any ground of rejection.

**Rejections under 35 U.S.C. § 102(b)**

The Action rejects claims 1-8, 20-21, 31, 33-34, and 39-41 as allegedly anticipated by Hirschbein, U.S. Pat. No. 5,166,387 (hereinafter referred to as the '387 patent); claims 1-6, 9-11, and 31-34 as allegedly anticipated by Caruthers *et al* ., U.S. Pat. No. 4,458,066 (hereinafter referred to as the '066 patent ); claims 1, 22-26, and 28-34 as allegedly anticipated by Caruthers *et al.*, U.S. Pat. No. 5,750,666 (hereinafter referred to as the '666 patent); and claims 1-7, 9-12, 20-21, 23-24, 28-31, 33-34, and 37-41 as allegedly anticipated by Ravikumar *et al.*, U.S. Pat. No. 5,614,621(hereinafter referred to as the '621 patent). Applicants respectfully traverse.

As the Examiner is well aware, for a rejection under § 102(b) to be properly founded, a single prior art reference must disclose, either expressly or inherently, each and every element of the claimed invention. *See, e.g., Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 231 USPQ 81 (Fed. Cir. 1986), *cert. denied*, 480 U.S. 947 (1987); and *Verdegaal Bros. V. Union Oil Co. Of California*, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). In *Scripps Clinic & Research Found. v. Genetech, Inc.*, 18 USPQ2d 1001 (Fed. Cir. 1991), the Federal Circuit held that:

> Invalidity for anticipation requires that all of the elements and limitations of the claim are found with a single prior art reference. . . .There must be no difference between the claimed invention and the reference disclosure, as viewed by a person of ordinary skill in the field of the invention. *Id.* at 1010.

Anticipation can be found, therefore, only when a cited reference discloses all of the elements, features, or limitations of the presently claimed invention.

The '387, '066, '666, and '621 patents do not disclose all of the elements of the presently claimed invention. The '387, '066, '666, and '621 patents discuss a method of synthesizing an oligomer wherein the oxidation and capping steps are carried out **in two separate steps**. For example, in column 4, lines 64-68 of the '387 patent, Hirschbein reports that the oxidation and

capping of the growing oligomer are performed in steps 3 and 4 respectively. In column 2, line 65 to column 3, line 5 of the '066 patent, Caruthers *et al.* report that the capping and oxidation of the growing oligomer are performed in sequential steps (b) and (c) respectively. In column 52, lines 53 to 65 of the '666 patent, Caruthers *et al.* report that the current synthetic cycle for phosphodiester polynucleotide synthesis consists of four steps. The capping and oxidation are carried out in separate steps 3 and 4. Finally, in column 7, lines 10-30 of the '621 patent, Ravikumar *et al.* report the oxidation of already capped phosphate compounds.

Methods of synthesizing an oligomer wherein the oxidation and capping steps are carried out **in two separate steps** do not anticipate the present claims which, in part, are directed to a method of synthesizing an oligomer wherein the oxidation and capping steps are carried out **in one single step.** For example, pending claim 1 is directed to synthesizing an oligomer wherein a 5'-O-protected compound is treated with a deprotecting reagent, coupled with an activated phosphorus composition, and subsequently treated with a mixture comprising an oxidizing reagent and capping reagent in a **single** step and for a time and under conditions effective to form an oligomeric compound. Accordingly, the oxidation of internucleoside linkages and capping of unreacted hydroxyl groups occurs simultaneously (*see* specification, page 23, line 33 to page 24, line 5).

In summary, as the cited references fail to teach all of the elements of the present invention, *i.e.*, the simultaneous oxidation of internucleoside linkages and capping of unreacted hydroxyl groups, Applicants respectfully request that the rejections under 35 U.S.C. § 102(b) be withdrawn.

**Rejections under 35 U.S.C. § 103(a)**

The Action rejects claims 13 and 14 as allegedly obvious over the '387 patent; claim 15 as allegedly obvious over the '666 patent or '066 patent in view of Santamaria *et al.*, U.S. Pat. No. 5,424,184 (hereinafter referred to as the '184 patent); and claims 37-38 as allegedly obvious over the '666 patent or '066 patent. in view of Krotz *et al.*, U.S. Pat. No. 6,399,765 B1 (hereinafter referred to as the '765 patent).

As is stated in M.P.E.P. § 2143, three criteria must be met to establish prima facie obviousness:

> First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

Here, a *prima facie* case of obviousness has not been established, at least because there is no suggestion or motivation to modify the references.

The Office Action fails to identify any motivation or suggestion in the cited references to combine the oxidation and capping process into one single step. Furthermore, there is no evidence of record suggesting the desirability or even possibility of such a combination. In fact, the cited references actually teach away from the present invention by presenting the common wisdom in the art, *i.e.*, that the capping and oxidation steps must take place in separate steps. (As previously discussed, see column 4, lines 64-68 of the '387 patent; column 2, line 65 to column 3, line 5 of the '066 patent; column 52, lines 53 to 65 of the '666 patent; and column 7, lines 10-30 of the '621 patent).

Accordingly, Applicants respectfully request that the rejection of claims 13-15 and 37-38 under 35 U.S.C. § 103 be withdrawn.

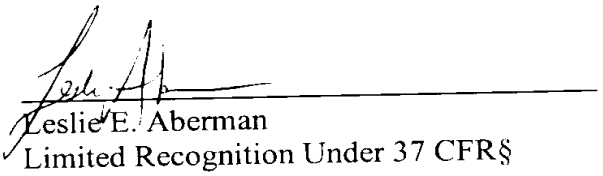
**Rejections under 35 U.S.C. § 112**

Claims 27 and 35-36 stand rejected under 35 U.S.C. § 112, second paragraph, as being allegedly indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In response, claim 1 has been amended to provide antecedent support for claim 27 and claim 35 has been amended to reflect the correct dependency. Accordingly, Applicants respectfully request the rejections under 35 U.S.C. § 112, second paragraph, be withdrawn.

The foregoing represents a *bona fide* attempt to advance the present case to allowance. Applicants submit that this application is now in condition for allowance. Accordingly, an indication of allowability and an early Notice of Allowance are respectfully requested.

Date: January 27, 2003



Leslie E. Aberman
Limited Recognition Under 37 CFR§ 10.9(b) attached

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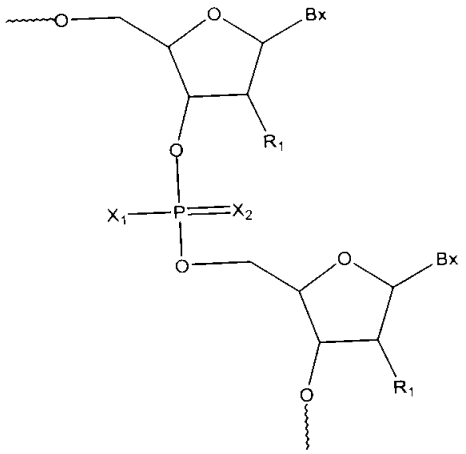
## APPENDIX A

## VERSION WITH MARKINGS TO SHOW CHANGES MADE TO THE CLAIMS

1. (Once Amended) A method of preparing an oligomeric compound having at least one moiety of formula:




wherein:

$X_2$ is O or S;

$X_1$ is Pg-O-, Pg-S-, $C_1$-$C_{10}$ straight or branched chain alkyl, $CH_3(CH2)_{nn}$-O-, $R_2R_3N$- or a group remaining from coupling a chiral auxiliary;

nn is from 0 to 10;

Pg is $CH_3$, -$CH_2CH_2CN$, -$C(CH_3)(CH_3)$-$CCl_3$, -$CH_2$-$CCl_3$, -$CH_2CH$=$CH_2$, $CH_2CH_2SiCH_3$, 2-yl-ethyl phenylsulfonate, δ-cyanobutenyl, cyano *p*-xylyl, diphenylsilylethyl, 4-nitro-2-yl-ethylbenzene, 2-yl-ethyl-methyl sulfonate, methyl-N-trifluoroacetyl ethyl, acetoxy phenoxy ethyl, or a blocking group;

[each $R_2$ and $R_3$ is, independently, hydrogen, $C_1$-$C_{10}$ alkyl, cycloalkyl or aryl;]

$R_1$ is, independently, hydrogen, a blocked hydroxyl group, a sugar substituent group, a nitrogen protecting group, a substituted or unsubstituted $C_1$-$C_{10}$ alkyl, a substituted or unsubstituted $C_2$-$C_{10}$ alkenyl, or a substituted or unsubstituted $C_2$-$C_{10}$ alkynyl, wherein said substitution is $OR_3$, $SR_3$, $NH_3$+, $N(R_3)(R_4)$, guanidine or acyl where said acyl is an acid amide or an ester;

$R_2$ is, independently, hydrogen, a $C_1$-$C_{10}$ alkyl, a cycloalkyl, an aryl, a nitrogen protecting group, a substituted or unsubstituted $C_1$-$C_{10}$ alkyl, a substituted or unsubstituted $C_2$-$C_{10}$ alkenyl, or a substituted or unsubstituted $C_2$-$C_{10}$ alkynyl, wherein said substitution is $OR_3$, $SR_3$, $NH_3$+, $N(R_3)(R_4)$, guanidine or acyl where said acyl is an acid amide or an ester;

or $R_1$ and $R_2$ together, are a nitrogen protecting group or are joined in a ring structure;

$R_3$ is hydrogen, a $C_1$-$C_{10}$ alkyl, a cycloalkyl, an aryl, or a nitrogen protecting group;

$R_4$ is, independently, $N(L_1)L_2$, hydrogen, a $C_1$-$C_{10}$ alkyl, or a nitrogen protecting group;

or $R_3$ and $R_4$, together, are a nitrogen protecting group;

or $R_3$ and $R_4$ are joined in a ring structure;

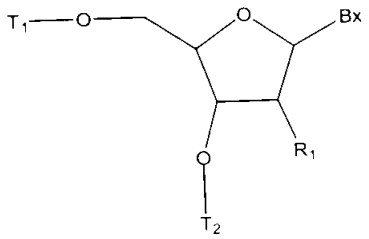
or optionally, $R_2$ and $R_3$, together with the nitrogen atom to which they are attached form a cyclic moiety;

each Bx is, independently, a heterocyclic base moiety; and

[each $R_1$ is, independently, H, a blocked hydroxyl group, or a sugar substituent group]

comprising the steps of:

(a) providing a 5'-O-protected compound of the formula:



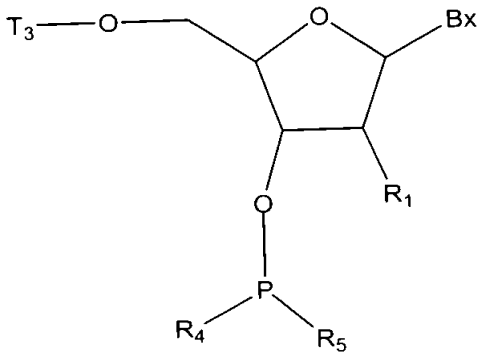

wherein:

$T_1$ is a hydroxyl protecting group; and

$T_2$ is a covalent attachment to a support media, a nucleoside bound to a support media, a nucleotide, an oligonucleoside or an oligonucleotide;

(b) treating said 5'-O-protected compound with a deprotecting reagent for a time and under conditions effective to form a 5'-O-deprotected compound;

(c) coupling said 5'-O-deprotected compound with an activated phosphorus composition of the formula:




wherein:

$T_3$ is a hydroxyl protecting group, a nucleoside, a nucleotide, an oligonucleoside or an oligonucleotide;

[$R_4$ is $N(L_1)L_2$]

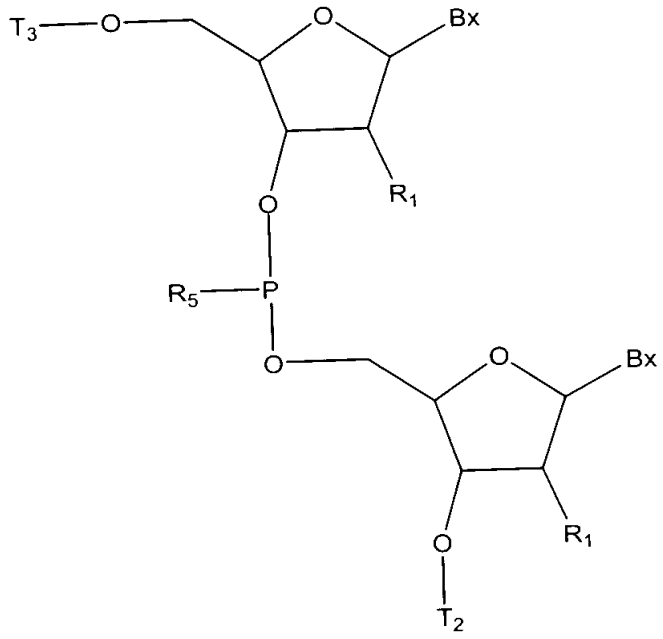
each $L_1$ and $L_2$ is, independently, $C_{1-6}$ straight or branched alkyl, or a $C_{5-7}$ cyclic aliphatic ring system;

or $L_1$ and $L_2$ are joined together to form a 4- to 13-membered heterocyclic ring system including the nitrogen atom to which L1 and L2 are attached; and

$R_5$ is $X_1$;

or $R_4$ and $R_5$ together with the phosphorus atom to which $R_4$ and $R_5$ are attached form a chiral auxiliary;

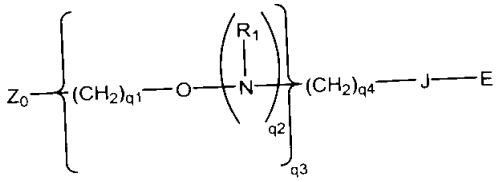
for a time and under conditions effective to form an extended compound having the formula:



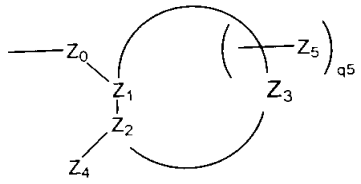

(d) treating said extended compound with a mixture comprising an oxidizing reagent and a capping reagent in a single step and for a time and under conditions effective to form said oligomeric compound.

27. (Once Amended) The method of claim 1 wherein each of said sugar substituent groups is, independently, $C_1$-$C_{20}$ alkyl, $C_2$-$C_{20}$ alkenyl, $C_2$-$C_{20}$ alkynyl, $C_5$-$C_{20}$ aryl, O-alkyl, O-alkenyl, O-alkynyl, O-aryl, O-aralkyl, O-alkylamino, O-alkylaminoalkyl (O-alkyl-N(H)alkyl), O-alkylaminodialkyl (O-alkyl-N-(alkyl)$_2$), O-alkylalkoxy (O-alkyl-O-alkyl), O-alkyl-(N-imidazole), thiol, S-alkyl, S-alkenyl, S-alkynyl, NH-alkyl, NH-alkenyl, NH-alkynyl, N-dialkyl, S-aryl, NH-aryl, S-aralkyl, NH-aralkyl, N-phthalimido, halogen keto, carboxyl, nitro, nitroso, nitrile, trifluoromethyl, trifluoromethoxy, N-imidazole, azido, hydrazino, hydroxylamino, isocyanato, sulfoxide, sulfone, sulfide, disulfide, silyl, heterocycle, carbocycle, polyamine, polyamide, polyalkylene glycol, or polyether;

or, alternatively, one or more substituent groups has one of formula I or II:




I



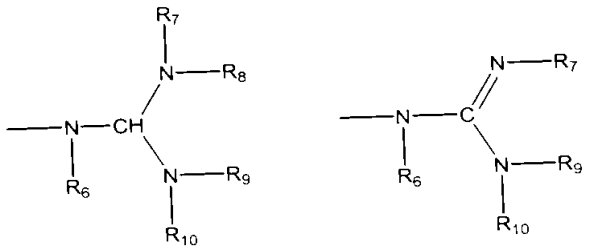

II

wherein:

$Z_0$ is O, S or NH;

J is a single bond, O or C(=O);

E is $C_1$-$C_{10}$ alkyl, $N(R_1)(R_2)$, $N(R_1)(R_5)$, $N=C(R_1)(R_2)$, $N=C(R_1)(R_5)$ or has one of formula III or IV;



III IV

each $R_6$, $R_7$, $R_8$, $R_9$ and $R_{10}$ is, independently, hydrogen, $C(O)R_{11}$, substituted or unsubstituted $C_1$-$C_{10}$ alkyl, substituted or unsubstituted $C_2$-$C_{10}$ alkenyl, substituted or unsubstituted $C_2$-$C_{10}$ alkynyl, alkylsulfonyl, arylsulfonyl, a chemical functional group or a conjugate group, wherein the substituent groups are selected from hydroxyl, amino, alkoxy, carboxy, benzyl, phenyl, nitro, thiol, thioalkoxy, halogen, alkyl, aryl, alkenyl and alkynyl;

or optionally, $R_7$ and $R_8$, together form a phthalimido moiety with the nitrogen atom to which they are attached;

or optionally, $R_9$ and $R_{10}$, together form a phthalimido moiety with the nitrogen atom to which they are attached;

each $R_{11}$ is, independently, substituted or unsubstituted $C_1$-$C_{10}$ alkyl, trifluoromethyl, cyanoethyloxy, methoxy, ethoxy, t-butoxy, allyloxy, 9-fluorenylmethoxy, 2-(trimethylsilyl)-ethoxy, 2,2,2-trichloroethoxy, benzyloxy, butyryl, iso-butyryl, phenyl or aryl;

$R_5$ is T-L,

T is a bond or a linking moiety;

L is a chemical functional group, a conjugate group or a support media;

each $R_1$ and $R_2$ is, independently, H, a nitrogen protecting group, substituted or unsubstituted $C_1$-$C_{10}$ alkyl, substituted or unsubstituted $C_2$-$C_{10}$ alkenyl, substituted or

unsubstituted $C_2$-$C_{10}$ alkynyl, wherein said substitution is $OR_3$, $SR_3$, $NH_3$+, $N(R_3)(R_4)$, guanidino or acyl where said acyl is an acid amide or an ester;

or $R_1$ and $R_2$, together, are a nitrogen protecting group or are joined in a ring structure that optionally includes an additional heteroatom selected from N and O;

or $R_1$, T and L, together, are a chemical functional group;

each $R_3$ and $R_4$ is, independently, H, $C_1$-$C_{10}$ alkyl, a nitrogen protecting group, or $R_3$ and $R_4$, together, are a nitrogen protecting group;

or $R_3$ and $R_4$ are joined in a ring structure that optionally includes an additional heteroatom selected from N and O;

$Z_4$ is OX, SX, or $N(X)_2$;

each X is, independently, H, $C_1$-$C_8$ alkyl, $C_1$-$C_8$ haloalkyl, $C(=NH)N(H)R_5$, $C(=O)N(H)R_5$ or $OC(=O)N(H)R_5$;

$R_5$ is H or $C_1$-$C_8$ alkyl;

$Z_1$, $Z_2$ and $Z_3$ comprise a ring system having from about 4 to about 7 carbon atoms or having from about 3 to about 6 carbon atoms and 1 or 2 hetero atoms wherein said hetero atoms are selected from oxygen, nitrogen and sulfur and wherein said ring system is aliphatic, unsaturated aliphatic, aromatic, or saturated or unsaturated heterocyclic;

$Z_5$ is alkyl or haloalkyl having 1 to about 10 carbon atoms, alkenyl having 2 to about 10 carbon atoms, alkynyl having 2 to about 10 carbon atoms, aryl having 6 to about 14 carbon atoms, $N(R_1)(R_2)$ $OR_1$, halo, $SR_1$ or CN;

each $q_1$ is, independently, an integer from 1 to 10;

each $q_2$ is, independently, 0 or 1;

$q_3$ is 0 or an integer from 1 to 10;

$q_4$ is an integer from 1 to 10;

$q_5$ is from 0, 1 or 2; and

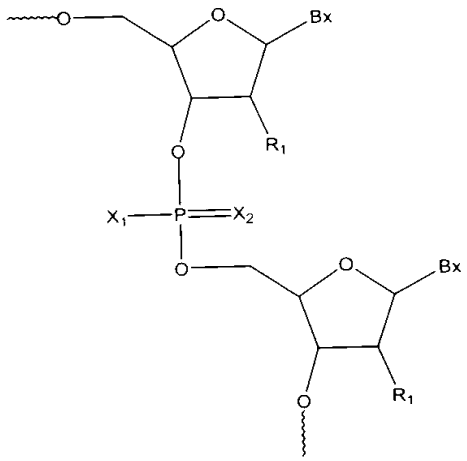
provided that when $q_3$ is 0, $q_4$ is greater than 1.

35. (Once Amended) The method of claim [32] 34 wherein said deprotecting reagent is dichloroacetic acid, trichloroacetic acid, zinc bromide, $AlC_3$, $TiC_4$, (Et)AlCl, (*I*-Bu)$_2$AlCl, ceric ammonium nitrate, 1,1,1,3,3,3-hexafluoro-2-propanol or diethyloxomalonate.

## APPENDIX B

## PENDING CLAIMS SUBJECT TO EXAMINATION

1. (Once Amended) A method of preparing an oligomeric compound having at least one moiety of formula:




wherein:

$X_2$ is O or S;

$X_1$ is Pg-O-, Pg-S-, $C_1$-$C_{10}$ straight or branched chain alkyl, $CH_3(CH2)_{nn}$-O-, $R_2R_3N$- or a group remaining from coupling a chiral auxiliary;

nn is from 0 to 10;

Pg is $CH_3$, -$CH_2CH_2CN$, -$C(CH_3)(CH_3)$-$CCl_3$, -$CH_2$-$CCl_3$, -$CH_2CH$=$CH_2$, $CH_2CH_2SiCH_3$, 2-yl-ethyl phenylsulfonate, δ-cyanobutenyl, cyano *p*-xylyl, diphenylsilylethyl, 4-nitro-2-yl-ethylbenzene, 2-yl-ethyl-methyl sulfonate, methyl-N-trifluoroacetyl ethyl, acetoxy phenoxy ethyl, or a blocking group;

$R_1$ is, independently, hydrogen, a blocked hydroxyl group, a sugar substituent group, a nitrogen protecting group, a substituted or unsubstituted $C_1$-$C_{10}$ alkyl, a substituted or unsubstituted $C_2$-$C_{10}$ alkenyl, or a substituted or unsubstituted $C_2$-$C_{10}$ alkynyl, wherein said substitution is $OR_3$, $SR_3$, $NH_3$+, $N(R_3)(R_4)$, guanidine or acyl where said acyl is an acid amide or an ester;

$R_2$ is, independently, hydrogen, a $C_1$-$C_{10}$ alkyl, a cycloalkyl, an aryl, a nitrogen protecting group, a substituted or unsubstituted $C_1$-$C_{10}$ alkyl, a substituted or unsubstituted $C_2$-$C_{10}$ alkenyl, or a substituted or unsubstituted $C_2$-$C_{10}$ alkynyl, wherein said substitution is $OR_3$, $SR_3$, $NH_3$+, $N(R_3)(R_4)$, guanidine or acyl where said acyl is an acid amide or an ester;

or $R_1$ and $R_2$ together, are a nitrogen protecting group or are joined in a ring structure;

$R_3$ is, independently, hydrogen, a $C_1$-$C_{10}$ alkyl, a cycloalkyl, an aryl, or a nitrogen protecting group;

$R_4$ is, independently, $N(L_1)L_2$, hydrogen, a $C_1$-$C_{10}$ alkyl, or a nitrogen protecting group;

or $R_3$ and $R_4$, together, are a nitrogen protecting group;

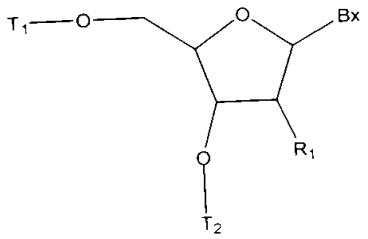
or $R_3$ and $R_4$ are joined in a ring structure;

or optionally, $R_2$ and $R_3$, together with the nitrogen atom to which they are attached form a cyclic moiety;

each Bx is, independently, a heterocyclic base moiety; and

comprising the steps of:

(a) providing a 5'-O-protected compound of the formula:



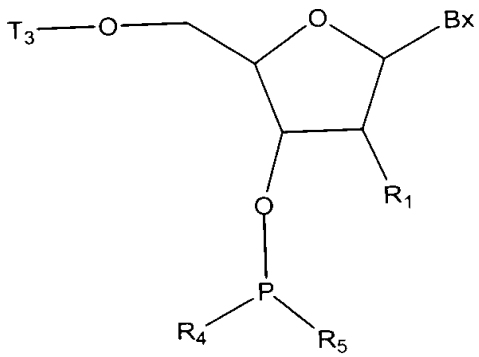

wherein:

$T_1$ is a hydroxyl protecting group; and

$T_2$ is a covalent attachment to a support media, a nucleoside bound to a support media, a nucleotide, an oligonucleoside or an oligonucleotide;

(b) treating said 5'-O-protected compound with a deprotecting reagent for a time and under conditions effective to form a 5'-O-deprotected compound;

(c) coupling said 5'-O-deprotected compound with an activated phosphorus composition of the formula:




wherein:

$T_3$ is a hydroxyl protecting group, a nucleoside, a nucleotide, an oligonucleoside or an oligonucleotide;

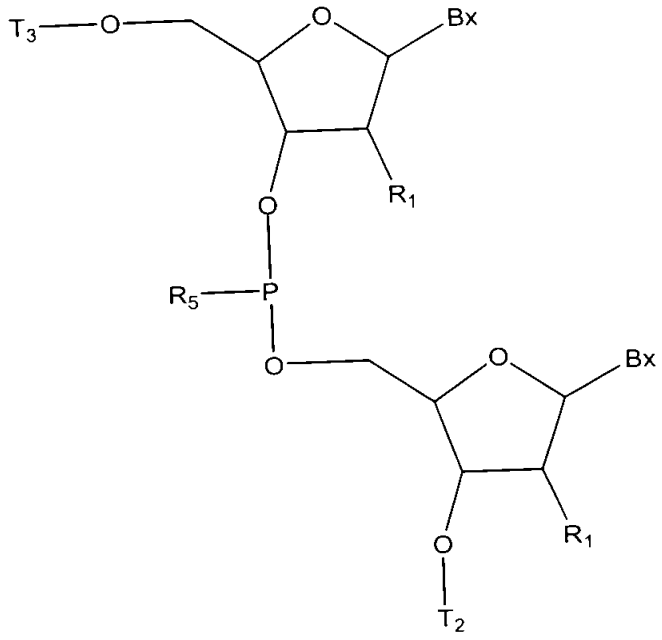
each $L_1$ and $L_2$ is, independently, $C_{1-6}$ straight or branched alkyl, or a $C_{5-7}$ cyclic aliphatic ring system;

or $L_1$ and $L_2$ are joined together to form a 4- to 13-membered heterocyclic ring system including the nitrogen atom to which L1 and L2 are attached; and

$R_5$ is $X_1$;

or $R_4$ and $R_5$ together with the phosphorus atom to which $R_4$ and $R_5$ are attached form a chiral auxiliary;

for a time and under conditions effective to form an extended compound having the formula:




(d) treating said extended compound with a mixture comprising an oxidizing reagent and a capping reagent in a single step and for a time and under conditions effective to form said oligomeric compound.

2. The method of claim 1 further comprising treating said oligomeric compound with a reagent for a time and under conditions effective to remove said blocking groups thereby forming a deblocked oligomeric compound.

3. The method of claim 2 wherein said reagent is effective to cleave the oligomeric compound from the support media.

4. The method of claim 3 wherein said reagent is aqueous ammonium hydroxide.

5. The method of claim 2 further comprising treating said oligomeric compound with a further reagent for a time and under conditions effective to cleave the oligomeric compound from the support media.

6. The method of claim 1 further comprising treating said oligomeric compound with a deprotecting reagent for a time and under conditions effective to deprotect the $T_3$ hydroxyl protecting group.

7. The method of claim 1 wherein said mixture comprises from 0.02M to 0.2M oxidizing reagent.

8. The method of claim 7 wherein said mixture comprises from 0.1M to 0.2M oxidizing reagent.

9. The method of claim 1 wherein said oxidizing reagent transfers an oxygen atom.

10. The method of claim 9 wherein said oxidizing reagent is iodine, *m*-chloroperbenzoic acid, iodobenzene diacetate, tetra-n-butylammonium periodate, *tert*-butyl hydroperoxide, di-*tert*-butyl hydroperoxide, cumene hydroperoxide, hydrogen peroxide; bis-trimethylsilyl peroxide; dinitrogen tetroxide, oxone, molecular oxygen, (1*S*)-(+)-(10-camphorsulfonyl)oxaziridine or a peracid.

11. The method of claim 10 wherein said oxidizing reagent is iodine, *m*-chloroperbenzoic acid, iodobenzene diacetate, *tert*-butyl hydroperoxide, di-*tert*-butyl hydroperoxide, hydrogen peroxide, oxone, molecular oxygen or a peracid.

12. The method of claim 1 wherein said oxidizing reagent transfers a sulfur atom.

13. The method of claim 12 wherein said oxidizing reagent is 3-amino-1,2,4-dithiazole-5-thione; 3-ethoxy-1,2,4-dithiazoline-5-one; 1,2,4-dithiazolidine-3,5-dione; 3-methyl-1,2,4-dithiazolin-5-one; or dimethylthiuram disulfide.

14. The method of claim 13 wherein said oxidizing reagent is dimethylthiuram disulfide.

15. The method of claim 1 wherein said capping reagent comprises about one part by volume of either acetic anhydride in acetonitrile or tetrahydrofuran; or chloroacetic anhydride in acetonitrile or tetrahydrofuran; added to about one part by volume of either N-methylimidazole and pyridine in acetonitrile or tetrahydrofuran; or *t*-butylphenoxyacetic anhydride in acetonitrile or tetrahydrofuran.

16. The method of claim 15 wherein said capping reagent comprises about one part by volume of 20% acetic anhydride in acetonitrile mixed with about one part by volume of a solution having 20% N-methylimidazole, 30% pyridine and 50% acetonitrile.

17. The method of claim 1 wherein said mixture comprises dimethylthiuram disulfide, acetic anhydride, acetonitrile, N-methyl imidazole and pyridine.

18. The method of claim 1 wherein said mixture comprises from about 0.05M to 0.2M dimethylthiuram disulfide, about 10% acetic anhydride, about 10% N-methyl imidazole and about 15% pyridine in a suitable solvent.

19. The method of claim 18 wherein said solvent is acetonitrile, toluene, ethyl acetate, tetrahydrofuran, dichloromethane, dichloroethane, dioxane, dimethylacetamide and dimethylformamide.

20. The method of claim 1 wherein said coupling of the 5'-O-deprotected compound with the activated phosphorus composition is performed in the presence of an activating agent.

21. The method of claim 20 wherein said activating agent is 1-H-tetrazole or 4,5-dicyanoimidazole.

22. The method of claim 1 where said cyclic moiety is morpholino or phthalimido.

23. The method of claim 1 wherein each $L_1$ and $L_2$ is $C_1$-$_6$ alkyl.

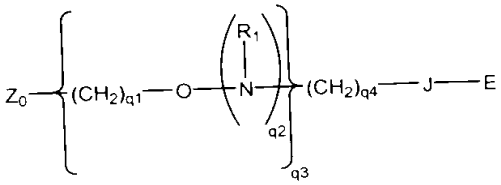
24. The method of claim 23 wherein each $L_1$ and $L_2$ is isopropyl.

25. The method of claim 1 wherein $L_1$ and $L_2$ are joined together to form a heterocyclic ring system including the nitrogen atom to which said $L_1$ and $L_2$ are attached, wherein said ring system optionally includes at least one additional heteroatom selected from O, N and S.

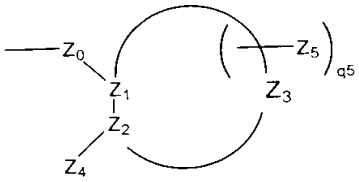
26. The method of claim 25 wherein said heterocyclic ring system is morpholino.

27. (Once Amended) The method of claim 1 wherein each of said sugar substituent groups is, independently, $C_1$-$C_{20}$ alkyl, $C_2$-$C_{20}$ alkenyl, $C_2$-$C_{20}$ alkynyl, $C_5$-$C_{20}$ aryl, O-alkyl, O-alkenyl, O-alkynyl, O-aryl, O-aralkyl, O-alkylamino, O-alkylaminoalkyl (O-alkyl-N(H)alkyl), O-alkylaminodialkyl (O-alkyl-N-(alkyl)$_2$), O-alkylalkoxy (O-alkyl-O-alkyl), O-alkyl-(N-imidazole), thiol, S-alkyl, S-alkenyl, S-alkynyl, NH-alkyl, NH-alkenyl, NH-alkynyl, N-dialkyl, S-aryl, NH-aryl, S-aralkyl, NH-aralkyl, N-phthalimido, halogen keto, carboxyl, nitro, nitroso, nitrile, trifluoromethyl, trifluoromethoxy, N-imidazole, azido, hydrazino, hydroxylamino, isocyanato, sulfoxide, sulfone, sulfide, disulfide, silyl, heterocycle, carbocycle, polyamine, polyamide, polyalkylene glycol, or polyether;

or, alternatively, one or more substituent groups has one of formula I or II:



I



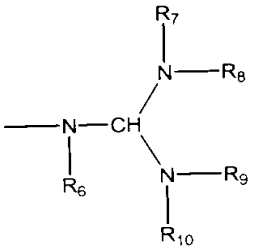
II

wherein:

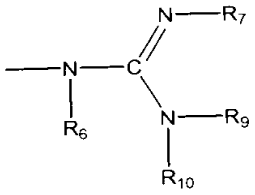
$Z_0$ is O, S or NH;

J is a single bond, O or C(=O);

E is $C_1$-$C_{10}$ alkyl, $N(R_1)(R_2)$, $N(R_1)(R_5)$, $N=C(R_1)(R_2)$, $N=C(R_1)(R_5)$ or has one of formula III or IV;



III



IV

each $R_6$, $R_7$, $R_8$, $R_9$ and $R_{10}$ is, independently, hydrogen, $C(O)R_{11}$, substituted or unsubstituted $C_1$-$C_{10}$ alkyl, substituted or unsubstituted $C_2$-$C_{10}$ alkenyl, substituted or unsubstituted $C_2$-$C_{10}$ alkynyl, alkylsulfonyl, arylsulfonyl, a chemical functional group or a conjugate group, wherein the substituent groups are selected from hydroxyl, amino, alkoxy, carboxy, benzyl, phenyl, nitro, thiol, thioalkoxy, halogen, alkyl, aryl, alkenyl and alkynyl;

or optionally, $R_7$ and $R_8$, together form a phthalimido moiety with the nitrogen atom to which they are attached;

or optionally, $R_9$ and $R_{10}$, together form a phthalimido moiety with the nitrogen atom to which they are attached;

each $R_{11}$ is, independently, substituted or unsubstituted $C_1$-$C_{10}$ alkyl, trifluoromethyl, cyanoethyloxy, methoxy, ethoxy, t-butoxy, allyloxy, 9-fluorenylmethoxy, 2-(trimethylsilyl)-ethoxy, 2,2,2-trichloroethoxy, benzyloxy, butyryl, iso-butyryl, phenyl or aryl;

$R_5$ is T-L,

T is a bond or a linking moiety;

L is a chemical functional group, a conjugate group or a support media;

each $R_1$ and $R_2$ is, independently, H, a nitrogen protecting group, substituted or unsubstituted $C_1$-$C_{10}$ alkyl, substituted or unsubstituted $C_2$-$C_{10}$ alkenyl, substituted or unsubstituted $C_2$-$C_{10}$ alkynyl, wherein said substitution is $OR_3$, $SR_3$, $NH_3$+, $N(R_3)(R_4)$, guanidino or acyl where said acyl is an acid amide or an ester;

or $R_1$ and $R_2$, together, are a nitrogen protecting group or are joined in a ring structure that optionally includes an additional heteroatom selected from N and O;

or $R_1$, T and L, together, are a chemical functional group;

each $R_3$ and $R_4$ is, independently, H, $C_1$-$C_{10}$ alkyl, a nitrogen protecting group, or $R_3$ and $R_4$, together, are a nitrogen protecting group;

or $R_3$ and $R_4$ are joined in a ring structure that optionally includes an additional heteroatom selected from N and O;

$Z_4$ is OX, SX, or $N(X)_2$;

each X is, independently, H, $C_1$-$C_8$ alkyl, $C_1$-$C_8$ haloalkyl, $C(=NH)N(H)R_5$, $C(=O)N(H)R_5$ or $OC(=O)N(H)R_5$;

$R_5$ is H or $C_1$-$C_8$ alkyl;

$Z_1$, $Z_2$ and $Z_3$ comprise a ring system having from about 4 to about 7 carbon atoms or having from about 3 to about 6 carbon atoms and 1 or 2 hetero atoms wherein said hetero atoms are selected from oxygen, nitrogen and sulfur and wherein said ring system is aliphatic, unsaturated aliphatic, aromatic, or saturated or unsaturated heterocyclic;

$Z_5$ is alkyl or haloalkyl having 1 to about 10 carbon atoms, alkenyl having 2 to about 10 carbon atoms, alkynyl having 2 to about 10 carbon atoms, aryl having 6 to about 14 carbon atoms, $N(R_1)(R_2)$ $OR_1$, halo, $SR_1$ or CN;

each $q_1$ is, independently, an integer from 1 to 10;

each $q_2$ is, independently, 0 or 1;

$q_3$ is 0 or an integer from 1 to 10;

$q_4$ is an integer from 1 to 10;

$q_5$ is from 0, 1 or 2; and

provided that when $q_3$ is 0, $q_4$ is greater than 1.

28. The method of claim 1 wherein said $X_1$ is Pg-O-, Pg-S-, $CH_3$-, $CH_3$-O-, morpholino or $R_2R_3N$- where each $R_2$ and $R_3$ is, independently, hydrogen or $C_1$-$C_{10}$ alkyl.

29. The method of claim 1 wherein said Pg is $CH_2CH_2CN$, diphenylsilylethyl, δ-cyanobutenyl, cyano p-xylyl, methyl-N-trifluoroacetyl ethyl or acetoxy phenoxy ethyl.

30. The method of claim 1 wherein said heterocyclic base moiety is adenine, $N^6$-benzoyladenine, cytosine, $N^4$-benzoylcytosine, 5-methylcytosine, $N^4$-benzoyl-5-methylcytosine, thymine, uracil, guanine, $N^2$-isobutyrylguanine or 2-aminoadenine.

31. The method of claim 1 wherein said support media bound nucleoside, nucleotide, oligonucleoside or oligonucleotide is blocked at reactive sites.

32. The method of claim 1 wherein said blocking groups are acid stable.

33. The method of claim 1 wherein said blocking groups are base labile.

34. The method of claim 1 wherein said deprotecting reagent is acidic, neutral or basic.

35. (Once Amended) The method of claim 34 wherein said deprotecting reagent is dichloroacetic acid, trichloroacetic acid, zinc bromide, $AlC_3$, $TiC_4$, (Et)AlCl, (*I*-Bu)$_2$AlCl, ceric ammonium nitrate, 1,1,1,3,3,3-hexafluoro-2-propanol or diethyloxomalonate.

36. The method of claim 35 wherein said deprotecting reagent is 2-5% dichloroacetic acid in dichloromethane or dichloroethane.

37. The method of claim 1 wherein said deprotecting reagent is a fluoride moiety.

38. The method of claim 37 wherein said fluoride moiety is $BF_3$-etherate.

39. The method of claim 1 wherein said oligomeric compound comprises from 5 to about 50 nucleosides.

40. The method of claim 1 wherein said oligomeric compound comprises from 8 to about 30 nucleosides.

41. The method of claim 1 wherein said oligomeric compound comprises from 15 to about 25 nucleosides.